LAPAROTOMY FOR FEVER

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The problems involved in the diagnosis of fever of uncertain or unknown origin are well known. In the majority of these patients, the diagnosis becomes established after a full investigation. Others no doubt are treated empirically and are considered to be cured because of the subsidence of the pyrexia. There are, however, cases where the most careful investigation fails to discover the cause even though the fever may have lasted months. It is indeed some of these patients who may benefit by a laparotomy not only because a definite diagnosis may result but also because a definitive cure becomes possible. The following two cases will illustrate this fact.

CASE 1

A.S. a 58 year old male from Valletta, was first seen by one of us (F.F.F.) on 1st April 1971 for recurrent fever of unknown origin. He gave a two to three years history of recurrent episodes of rigors with fever up to 101°F and on occasion up to 103°F lasting two or three days. These episodes were becoming more frequent. He had been given several courses of penicillin by his doctor. A careful history elicited a few other symptoms, namely early morning cough with some whitish expectoration, which was occasionally purulent and mild exertional dyspnoea on moderate effort with occasional substernal discomfort. There was no loss of appetite or weight. Over the past year or two, he passed frank red blood per rectum with his stools at times — ascribed to piles — but his bowels were open normally otherwise. There was no disturbance of micturition apart from nocturia x 1. He had lately become somewhat hard of hearing. He smoked 20 cigarettes daily and drank moderately. He was stated to have had hereditary spirochaetal infection and had also had some treatment for hiatus hernia in the past. He had suffered from sciatica.

Clinical examination revealed a somewhat obese but otherwise healthy middle aged man. There was no abnormality whatever in any system. His temperature was 100.8°F and his blood pressure was 130/80. The investigations carried out included:- full blood counts, serum electrolytes, blood urea, blood cultures, agglutinins titration: all negative or within normal limits. RPCF, Kahn's and VDRL tests were negative, so were urine analysis and culture. ESR was 30 mm/hr. Culture of the sputum elicited some mixed flora; while cytology showed squamous metaplastic changes but no evidence of malignancy. Test for occult blood in the faeces was positive. An X-Ray Chest and E.C.G. were within the normal. A barium meal and follow through simply confirmed the presence of hiatus hernia.

The patient had been admitted on two occasions for a few days but was being investigated mainly as an out patient. By now it was late June 1971. As he still had slight bleeding per rectum off and on, a barium enema was carried out and it showed a polypoidal filling defect in the sigmoid region with irregular margins suggesting possible malignancy. Rectal examination of the patient yielded blood stained faeces at this stage. Finally, an IVP was carried out but the only abnormality here was slight prostatic indentation in base of bladder. It was decided to

deal with the lesion in the colon and of course at the same time thoroughly explore the abdominal cavity.

At laparotomy (R.A.) on 26th July 1971, thorough exploration revealed only a growth of the sigmoid colon with no obvious extension beyond the organ. A pelvic colectomy was carried out with end to end anastomosis and a rectal tube was used for decompression as described elsewhere (Attard R. 1972). No other cause for the recurrent fever was found anywhere in the abdomen. The histology report relates that sections showed proliferative pinkish grey tumour tissue in the lumen over a length of 13 cms. The lymph nodes were not enlarged. Microscopical examination showed adenocarcinoma with little mucus formation. Mitotic activity was marked but there was no muscle infiltration. The patient was somewhat chesty postoperatively but he made an excellent recovery and was discharged on 10th August 1971. He has remained very well since then and when seen last week stated he had not had fever since the operation.

CASE 2

J.V., a 51 year old man from Naxxar, was first admitted under the care of one of us (F.F.F.) on 20th August 1970 for "orchitis". He had had three episodes of fever up to 101°F and pain over the lumbar spine in the previous six months accompanied by profuse night sweating. He also complained of loss of appetite and weight as well as bilateral somewhat painful testicular swellings. Further questioning elicited the presence of a non-productive hacking cough over some months possibly years, and also nausea and vomiting on occasion. There was slight dysuria. His bowels were open regularly. He did not smoke or drink. The patient stated he had had some rheumatic joint pains four years prior to the present condition.

On clinical examination, he was found to have only slightly enlarged tender testes. A blood count was within normal limits, urine analysis showed traces of protein and a chest X-ray showed prominent hilary shadows. The patient was an anxious man who did not like staying in hospital. So he was discharged on 5th September 1970 to be followed up in Out-Patients' Clinic. But he did not turn up till he was readmitted on 17th February 1971. He said the testicular swellings had subsided some three months after he had been previously discharged. However, he was still getting intermittent bouts of fever going up to 101°F in the evenings with malaise, anorexia and night sweats. The dry cough was still present and the right testis was a little painful. On examination, he had a temperature of 99°F, a Blood Pressure of 135/80 and a slightly tender right testis. His liver was just palpable. There were no other positive findings. The investigations were as follows: Hb was in the region of 8 to 9 G. on repeated testis but the differential count was within normal limits and total WBC was in the region of 7000/c.m. Reticulocytes 1.4%; ESR 110mm/hr. Blood urea ranged from 60 to 72mg/100ml. Serum electrolytes were normal. Tests for agglutinins were negative on three occasions. (Serum electrophoresis showed the pattern of an inflammatory process associated with diabetes — though he was not a diabetic). Urinalysis showed no abnormality except for calcium oxalate crystals and urine culture was negative both for the usual pathogens and for mycobacteria. Culture of sputum revealed no particular pathogens and a Chest X-ray was now passed as clean. Tests for occult blood in stools were positive on one and negative on two occasions.

As well as repeating these tests others were carried out. Liver function tests were within the normal. Blood for culture taken during bouts of fever on five different occasions was persistently negative. Coomb's test was negative. About a month after admission, his temperature was fluctuating between 100° and 103°F and his ESR was 130mm/hr., though at times it dropped to 50mm/hr. Haemoglobin electrophoresis was normal. An IVP (11.3.71) showed an enlargement of the spleen in the plain film and malrotation of the left kidney in the urography but no other abnormality. A barium meal (24.3.71) showed a hiatus her-

nia. A bone marrow examination revealed only definite features of an iron deficiency anaemia. During this period, he had had empirical treatment with penicillin and streptomycin (at home), ampicillin, salicylates, iron and folic acid preparations to no avail. The patient was finally persuaded to undergo an exploratory laparatomy after being given two units of blood.

At operation on 26.4.71 (R.A.), the spleen was found to be much enlarged, especially posteriorly and medially, entirely within the deep chested rib cage. It was turgid, smooth, diffusely mottled with small hard yellowish-white nodules. It weighed 1.28 kg (the normal spleen weighs not more then 200 mg.) and measured 18 × 17 × 11cm. Nodules similar to those on the surface were diffusely distributed within the pulp and were variable in size and shape. Microscopy showed malignant lymphoma with Sternberg-Reed cells, binucleated as well as multinucleated. Reticulum, lymphoid, plasma cells were arranged with sarcomatous cells to form a nodular pattern that replaced splenic pulp. Diagnosis:- Hodgkin's Disease. The temperature fell straight after the operation but was up again the following day and continued.

On the 21st May 1971, he was started on monthly courses of the four drugs: endoxan, velbe, prednisone and nitrogen mustard. This controlled the fever and his general state improved. However, 17 months later, in October 1972, he was still having bouts of fever, his ESR was 138mm/hr. and the Haemoglobin 10G., inspite of continued treatment. He died in November 1972.

Discussion

Sheon and Van Ommen (1963) state that the fever of undetermined origin that may well require laparotomy for its elucidation should have three characteristics: that it is over 38°C (100.5°F), lasts longer than three weeks and has remained undiagnosed after extensive investigations. Case 2 above fits these three characteristics completely. While in Case 1 a probable cancer of the sigmond colon was discovered preoperatively, it was only laparatomy thet excluded other causes of fever and in fact helped to cure the patient as well of the cancer. There is no doubt that the carrying out of laparotomy should be the final court of appeal, the last logical step in the series of investigations for fever of unknown origin, which may be caused by a large range of 'conditions' grouped as: infections, malignant tumours, collagen diseases, allergic disorders, metabolic disorders, endocrine disorders and in some instances factitiously (Ben-Shoshan, *et al;* 1971). Petersdorf and Beeson (1961) in a study of 100 unselected patients with fever of unknown origin found that 19 had intra-abdominal pathological conditions. Apart from the characteristics of the fever already mentioned, one should look for other clues as to possible intra-abdominal disorder in order to help one to decide on laparotomy. Such clues include anorexia, loss of weight, anaemia (BMJ Editorial, 1971); a positive intra-abdominal finding like enlarged liver or spleen (Keller and Williams, 1965); biochemical abnormality, especially altered liver function tests (Keller & Williams 1965; Ben-Shoshan *et al* 1971; Moossa and Skinner 1972). Indeed these workers consider the serum alkaline phosphatase to be the single most helpful test, though altered BSP retention and albumen/globulin ratios may also be significant. It should be emphasized that abnormal liver function tests in this context are not at all necessarily indicative of liver disorder but more particularly of positive intra-abdominal disease. A full radiological examination of gastrointestinal and genitourinary tracts is essential in all these patients.

In the largest series so far, Geraci *et al.* (1959) published a study of 70 cases of fever of obscure_origin who underwent laparotomy with 80% positive results, Kel ler and Williams (1965) in a similar study of 46 cases had 82% positive laparotomy results while Ben-Shoshan *et al.* (1971) had 70% positive results in 23 patients. Hence laparotomy solves the problem of fever of unknown origin in over two thirds of the patients. Of these 40% are found to have malignant diseases and another 40% intra-abdominal infection. In spite of the possible risks of operation, its value is clear. Indeed, a negative laparotomy result may also be a worthwhile contribution to the management of the patient.

It is interesting to note that almost all

the series of cases mentioned (Geraci *et al* 1959; Sheon and Van Ommen, 1963; Keller and Williams, 1965, and Ben-Shoshan *et al* 1971) included among their patients with fever of unknown origin not only cases with lymphoma or Hodgkin's but also from one to three cases of cancer of the colon. Clanton (1950) remarks that it is sometimes forgotten that fever is often a symptom of cancer. In fact, in 70.3% of his series of 64 patients with cancer of the colon and rectum there was fever not otherwise explained and indeed 4.9% of these patients had fever as the only symptom of cancer of the colon. The fever may be due to toxic degeneration of the cancer or to secondary infection, especially in fungating, ulcerating lesions as in Case 1 above. (Bacon, H.E. 1949). While fever as the prominent symptom of Cancer of the colon was the most interesting feature of Case 1, the fact that such a grossly enlarged spleen was impalpable in Case 2 contributed in very large measure to the obscurity of the fever. In each case, the vital clue was provided by the radiologist, as seen in retrospect.

In conclusion, the above two cases of fever are but unusual clinical syndromes of otherwise commonly known diseases (Geraci *et al).* They show that laparotomy may at the very least provide definite diagnosis of an intraabdominal disorder allowing rational management of the patient and may also in the best of cases cure such disorder.

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